

reasons which are stated in the July 30, 2002 office action. Essentially it is the Examiner's view that the use of the term "providing" and "symptoms of diabetes" in claim 22 renders that claim indefinite. Applicants respectfully traverse the Examiner's rejection.

Claim 22 very clearly indicates the method which Applicants regard as their invention. Claim 22 very deliberately and specifically set forth that the invention comprises 1). providing a therapeutically effective amount of conjugated linoleic acid and a human patient suffering from diabetes and administering the therapeutically effective amount of conjugated linoleic acid to the human diabetic patient under conditions such that the symptoms of diabetes are treated. The term "providing" is a generic term used in the art essentially as a presenting step in which the conjugated linoleic acid and the patient to be treated are presented together for administration. It is a step which necessarily precedes a step of administration by an individual other than the subject *per se*. The administering person may be a healthcare worker, a pharmacist, a physician or anyone other than the subject who presents the subject and the conjugated linoleic acid together for the subsequent administration step. It is respectfully submitted that this step is a clear, concise step and does not in any way render the method of claim 22 indefinite.

With respect to the phrase "symptoms of diabetes", this term clearly reflects the disclosure of the instant application on page 14 through to the top of page 15, as well as throughout the specification of the present application. Symptoms of diabetes include, for example, decreased glucose tolerance, increase in the blood levels of insulin and/or an increase in the level of circulating free fatty acids or triglycerides. These are clearly indicated as being treated by the method of the present invention. Thus, symptoms of diabetes are treated by the method of the present invention. It is respectfully submitted that the terms which have been rejected by the Examiner as being indefinite are clearly definite and are used in compliance with the requirements of 35 U.S.C. §112, second paragraph. We now turn to the Examiner's §103 rejection.

The §103 Rejection

The Examiner has rejected claims 1-22 under 35 U.S.C. §103 as being obvious over de Boer, et al., U.S. patent no. 5,518,751 ("de Boer"), in view of Cook, et al., U.S. patent no. 5,554,646 ("Cook"). It is the Examiner's position that de Boer teaches that CLA in food compositions such as milk are useful in treating disorders such as diabetes. The Examiner points to column 1, lines 35-43 in support of that view. The Examiner recognizes that de Boer does not teach particularly that CLA is useful in a method of treating diabetes, the specific conjugated linoleic acids claimed or the amount of CLA of the present invention. The Examiner cites Cook for teaching a method of adding linoleic acid compounds into animal feed to reduce fat in an animal and that specific isomers of octadecadienoic acid may be included in the conjugated linoleic acid.

From the teachings of the cited art the Examiner concludes that it would have been obvious to employ CLA in a method of treating diabetes and that it would have been obvious for one of ordinary skill in the art at the time the invention was made to incorporate about 1 mg to about 10,000mg/kg of body weight of the *trans,cis*-9,11-octadecadienoic acid, *cis,cis*-9,11-octadecadienoic acid or *trans,cis*-10,12-octadecadienoic acid into a milk composition product useful in a method of treating diabetes. The Examiner further argues that one of ordinary skill would have been motivated to employ CLA in a method of treating diabetes because de Boer, et al. Clearly teaches unsaturated fatty acids, preferably CLA, are useful in treating disorders including diabetes. It is the Examiner's conclusion, therefore, that one of ordinary skill would have reasonably *expected* that CLA would have been useful in a method of treating diabetes. Applicants respectfully traverse the Examiner's rejection.

It is respectfully submitted that the Examiner has not made out a cogent case for obviousness. Indeed, it is respectfully submitted that the Examiner has seized on a brief, *ambiguous* statement in the background section of a U.S. patent to de Boer which does not teach

or suggest the use of CLA for treating diabetes and combined that ambiguous disclosure with the teachings of Cook which are directed to using CLA to prevent or treat the adverse effects of antibody based hypersensitivity (attenuating the allergic response of Animals), to argue that the claimed invention is obvious. As will be argued in detail herein, the Examiner's argument is not cogent and represents a rejection based upon an impermissible *hindsight* reconstruction of the teachings of the two references in rendering the present invention obvious.

de Boer Does Not Teach or Suggest the Use of CLA for Treating Diabetes

Contrary to the Examiner's conclusions regarding the teachings of de Boer, de Boer *does not* disclose or suggest the use of CLA for the treatment of diabetes. In contrast, de Boer merely reiterates and summarizes the state of the art at the time of the filing of de Boer (September 8, 1994), *which did not recognize the significance of conjugated linoleic acid in the treatment of diabetes.* Contrary to what the Examiner has posited in making the rejection, the art clearly did not teach or suggest the use of CLA as a treatment modality for diabetes. Indeed, prior to the present application, it was not known that CLA, in contrast to γ -linolenic acid (GLA, commonly found in evening primrose oil, for example), could be used to treat diabetes.

The Examiner has cited no art, separate from the ambiguous disclosure in the background section of deBoer, which even arguably teaches or suggests the use of CLA for the treatment of diabetes. Thus, in context, given the ambiguous nature of the disclosure on which the Examiner relies, the Examiner's construction of the ambiguous disclosure must fail. Moreover, it is respectfully submitted that the Examiner is engaging in *impermissible hindsight reconstruction* of the ambiguous teachings of the art to somehow justify that the present invention is obvious. Note that at the time of the filing of the application, certain fatty acids were known to be useful in the treatment of diabetes (see above). However, prior to the present application, CLA was not known to be useful for treating diabetes, although it was known for the treatment of other conditions, which are actually set forth in the disclosure of deBoer. Indeed, the Examiner must

contort the ambiguous disclosure of deBoer because the art actually failed to appreciate the present invention. Prior to the present application, CLA was not known as a treatment modality for diabetes, and indeed, the first report in the literature of the significance of CLA in the treatment of diabetes, was Applicants' own paper, *Biochem Biophys Res Commun*, March 27, 244(3) 678-682 (1998). The date of Applicants' paper is some four (4) years after the filing date of de Boer. Prior to the present application, CLA was known for its anti-carcinogenic and anti-atherogenic properties having cardiovascular implications. Also known in the art was that α -linolenic acid and linoleic acid possesses properties which make it potentially useful in the treatment of cardiovascular disease (as indicated by de Boer). Thus, the disclosure in de Boer at column 1, lines 35-43, is completely consistent with the conventional understanding at the time of the filing of that reference and refers to the fact that it was known in the art to use linolenic acid in cardiovascular diseases and diabetes. It was, however, not known in the art before the present invention, that CLA could be used for the *treatment of diabetes or that CLA administration is a particularly effective treatment for diabetes*. Despite Applicants' requests in previous papers to have the Examiner cite *any reference* other than deBoer in support of the contention that the use of CLA in the treatment of deBoer teaches the use of CLA, the Examiner has not been able to cite such a reference. That is because such a reference does not exist.

The ambiguous passage in de Boer, which the Examiner relies on for the teaching that CLA may be used to treat diabetes is found in the background of the invention section at column 1, lines 35-43 and is presented below:

"An important reason for enriching milk or milk powders with fats containing a high percentage of unsaturated fatty acids or strongly unsaturated fatty acids is to prevent or reduce cardiovascular diseases, atrophies, rheumatic disorders or diabetes. In particular, such products contain a high percentage of oleic acid, linoleic acid which may or may not be conjugated, α -linolenic acid and unsaturated C₂₀ and C₂₂ fatty acids."

A fair reading of that ambiguous passage in the BACKGROUND OF THE INVENTION

section of de Boer is that de Boer is merely reviewing the conventional understanding at the time of the filing of de Boer which failed to appreciate the particularly effective use CLA could have in treating diabetes. Thus, it may be accurately argued and concluded, that de Boer merely reiterates a broad discussion of the art which did not teach or suggest the use of CLA for the treatment of diabetes, but rather the use of one or more of the disclosed fatty acids to treat the indicated conditions. It is again noted that, despite Applicants' several requests, the Examiner has failed to clear up the ambiguous disclosure of deBoer and has not separately cited any reference which actually teaches or suggests the use of CLA for the treatment of diabetes and instead, relies on the deficient disclosure of de Boer to make the rejection. Thus, de Boer does not teach the use of CLA for the treatment of diabetes, because the use of CLA to treat diabetes was first disclosed in the present application, well after de Boer. Again, Applicants challenge the Examiner to clarify the ambiguous disclosure of de Boer and actually cite a prior art reference which teaches the use of CLA for the treatment of diabetes.

Cook Does Not Obviate the Deficiencies of de Boer

Turning to the disclosure of Cook, this reference discloses a method of using CLA to reduce an immunogenic (allergic) response in animals, including humans. Although this reference supports the view that CLA may be used to attenuate a humoral immunogenic response (and thus, allergies) and/or to increase the white blood cell count in a mammal, there is absolutely no disclosure or suggestion of the use of CLA in the treatment of diabetes. Indeed, other than the fact that Cook suggests that CLA may be included in an animals diet, the relevance of Cook has not been made clear to Applicants.

It is respectfully submitted that a combination of de Boer and Cook does not disclose or suggest the present invention and that these references, in combination, only become relevant to the present invention *after one has read the instant application*. Thus, the Examiner's rejection is an example of impermissible hindsight reconstruction, a rejection which is clearly

impermissible under the law. See MPEP §706.02(j) and *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). This is especially true where, as here, the prior art, *in general*, does not disclose or suggest the claimed invention, and the Examiner relies for such teaching, on an ambiguous description of the prior art. As was stated in *In re Vaeck*, “the teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art and not based on applicant’s disclosure.” *In re Vaeck*, at 20 USPQ2d 1438,1442. In the present application, the Examiner has seized upon the ambiguous disclosure in de Boer, and **with impermissible reference to Applicants’ disclosure and teachings**, has concluded that de Boer teaches the present invention. **The Examiner’s analysis therefore represents a classical case of hindsight reconstruction to make an obviousness rejection- an analysis which the Court of Appeals for the Federal Circuit has found to be impermissible.**

In the present application, there is simply no cogent basis upon which to suggest that the prior art taught the use of CLA for the treatment of diabetes. While the disclosure in de Boer is unclear, the remaining art cited, Cook, is *inapposite* to the teaching. Yet, the Examiner, recognizing the deficiencies in the art, does not separately posit a prior art reference which teaches the use of CLA for the treatment of diabetes- that is because no independent basis exists. Applicants have respectfully requested the Examiner to cite whatever prior art may be available for the teaching that CLA is a particularly effective treatment for diabetes, independent of the ambiguous disclosure of de Boer. If the Examiner cannot make such a recitation, Applicants respectfully request the Examiner to withdraw the rejection of the present application.

The Examiner has also rejected claims 1-22 under 35 U.S.C. §103 as being obvious over Semenkovich and Heinecke, *Diabetes*, 1997, 46:327-334 (“Semenkovich”), in view of Steinhart, *Journal of Chemical Education*, 1996, 73(12):A302 and Cook (see above).

The Examiner cites Semenkovich for teaching that most diabetic patients die from macrovascular complications and that oxidative modification of lipoproteins in diabetic patients

is enhanced, with this being one of the major risks for developing cardiovascular complications (macrovascular complications) in diabetic patients. Semenkovich is also cited for teaching that antioxidants are potent inhibitors of lipoprotein lipid peroxidation and thereby reduce the lipoprotein oxidation products and cytotoxicity caused by those products. The Examiner acknowledges that Semenkovich does not expressly teach the employment of CLA in a method to treat diabetes or the symptoms of diabetes or the specific isomers of octadecaenoic acid or amounts of CLA.

The Examiner cites Steinhart for teaching CLA as a natural antioxidant. Cook is cited for teaching a method of adding CLA to animal feed.

From the disclosures of Semenkovich, Steinhart and Cook as set forth in the office action, the Examiner contends that the present invention is obvious and therefore, unpatentable. Applicants respectfully traverse the Examiner's rejection. A combination of these references in no way teaches or suggests that CLA was known or would have been expected to be a particularly effective treatment for diabetes.

Semenkovich is a reference which describes the relationship between diabetes and atherosclerosis, noting that in the vast majority of cases, individuals which exhibit symptoms of diabetes do not, in fact, develop premature vascular disease. See page 327 of Semenkovich, second column. In addition to the somewhat limited connection between diabetes and atherosclerosis is the fact that the mechanism for development of premature vascular disease is not particularly well understood. Indeed the title of the Semenkovich article is *"The Mystery of Diabetes and Atherosclerosis Time for a New Plot."* While Semenkovich teaches that antioxidants may be useful in addressing issues associated with oxidized lipoproteins in the development of atherogenesis, there is absolutely no disclosure that CLA in particular would be useful in the treatment of diabetes. Even a suggestion in Semenkovich that antioxidants might be useful in reducing lipoprotein oxidation products and therefore, may play a beneficial role in

limiting atherogenesis, there is no evidence that CLA as an antioxidant could play such a role. See, for the example, the enclosed Abstract of Berliner and Heinecke, *Free Radic. Biol. Med.*, 1996, 20(5):707-727 ("Berliner"), cited in Semenkovich (note 64), which clearly indicates that the mechanism of oxidation of lipoprotein is promoted by several different systems, including protein-bound metal ions, thios, reactive oxygen intermediates, lipoxygenase, peroxynitrite and myeloperoxidase. While Semenkovich may suggest the generic use of antioxidants to treat macrovascular disease in those limited number of diabetic patients in which such a condition occurs, there is absolutely no suggestion in Semenkovich that CLA should be used to treat diabetes *per se*. Noted here is the fact that even Semenkovich acknowledges that only a limited number of diabetic patients actually are at risk for macrovascular disease, most likely based upon some genetic predisposition. A limited disclosure, Semenkovich cannot possibly be read to suggest the use of CLA as a treatment modality for diabetes. It cannot even be fairly said that Semenkovich suggests CLA as a treatment modality for macrovascular disease, because it is not clear from the disclosure of Semenkovich (which cites Berliner) or from Berliner itself, that CLA would be a particularly effective antioxidant, given the lack of understanding of the oxidative process in producing such a condition. Semenkovich is clearly a deficient reference.

Steinhart does absolutely nothing to cure the deficiencies of Semenkovich, other than to suggest that CLA may be useful to treat macrovascular disease, which occurs in a limited number of diabetic patients. Steinhart discloses generally, that CLA is a natural antioxidant, which has important uses in the limitation of carcinogenesis and in certain instances, atherogenesis. Combining Semenkovich with Steinhart at best, merely suggests that CLA may be useful to treat atherogenesis. There is absolutely no disclosure or suggestion in Steinhart that CLA is useful for the treatment of diabetes.

Turning to Cook, it cannot be said that Cook somehow obviates a combined disclosure in Semenkovich and Cook in failing to suggest the present invention. Cook has been discussed supra, and that discussion is referenced here. Cook teaches that CLA may be used to limit

humoral based allergic reactions or to decrease white blood counts. There is not even an oblique reference in Cook to diabetes. Cook is inapposite to this discussion.

Combining the disclosures of Semenkovich, Steinhart and Cook does not result in a suggestion of the present invention. At best, such a combination suggests that CLA might be used to treat atherosclerosis in a limited number of diabetic patients. But that does not suggest the use of CLA for the treatment of diabetes *per se*. Such a combination of teachings cannot even make out an arguable case that the present invention is inherently disclosed, because such as rejection would have to rely on more than one reference (impermissible to an inherency rejection) and the teaching would not *inevitably and always* result in the claimed invention. Thus, the present invention is clearly patentable over the references cited by the Examiner.

For the above reasons, Applicant respectfully asserts that the claims set forth in the present amendment are now in compliance with 35 U.S.C. Applicants respectfully submit that the present application is now in condition for allowance and such action is earnestly solicited.

Applicant has neither cancelled nor added any claims. No fee is therefore due for the presentation of this amendment. A petition for an extension of time (one month) is enclosed as is a check for \$55.00. A copy of the abstract of Berliner, discussed herein, is attached as is an information disclosure statement, which Applicants respectfully request the Examiner to consider. Small entity status is claimed for the present application.

Please credit any overpayment or charge any additional fee due to Deposit Account No.
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Respectfully submitted,

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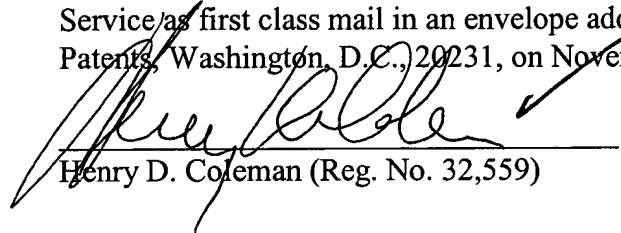
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APPENDIX

No amendments have been made to the claims of the instant application. Previously filed claims 1-22 remain pending in the present application.